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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/550,857	04/17/2000	Thomas Buch-Rasmussen	NN 26	1708

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PATENT DEPARTMENT
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EXAMINER	
YOUNG, JOSEPHINE	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/550,857	Applicant(s) BUCH-RASMUSSEN ET AL.	
	Examiner Josephine Young	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-14,16-35 and 39-59* is/are pending in the application.

4a) Of the above claim(s) *56-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-14,16-35,39-55 and 59* is/are rejected.

7)☒ Claim(s) *6,41 and 55* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Request for Continued Examination

The Request for Continued Examination (RCE) under 37 CFR 1.114 filed on April 7, 2003, is acknowledged.

Objections/Rejections Set Forth in the Office Action dated November 19, 2002

Claims 56-58 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

The oath or declaration was objected to as being defective because non-initialed and/or non-dated alterations have been made to the oath or declaration.

The Drawings were objected to as being informal because only photocopies of black and white photographs were submitted.

The Specification was objected to for use of the registered trademark "Maltidex H16323" without being capitalized wherever it appears and/or being accompanied by generic terminology.

Claim 6 was objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, namely claim 3.

Claims 1-14, 16-35, 39, 52-55 and 59 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-14, 16-35, 39-55 and 59 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-14, 16-35, 39-55 and 59 were rejected under 35 U.S.C. 103(a) as being unpatentable over International Publication No. WO 96/03978 to ROSER et al.

Claims 1-14, 16-35, 39-55 and 59 were rejected under 35 U.S.C. 103(a) as being unpatentable over ROSER in view of International Publication WO 94/22423 to BAR-SHALOM.

Response to the Amendment filed April 7, 2003

In the amendment filed April 7, 2003, the Specification was amended to delete the Figures and the Brief Description of the Figures. Further, the Specification was amended such that the registered trademark "Maltidex H16323" is clearly marked with a "®" and followed by generic terminology

Claim 1 was amended. Claim 8 was cancelled.

An action on the merits of claims 1-7, 9-14, 16-35, 38-55 and 59 is contained herein below.

In regards to the Objection to the oath or declaration, Applicant's new declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date filed April 7, 2003 has been fully considered and has overcome the Objection set forth in the Office Action dated November 19, 2002.

In regards to the Objection to the Drawings, Applicants' amendments filed April 7, 2003 have been fully considered and have overcome the Objection set forth in the Office Action dated November 19, 2002 (Drawings withdrawn).

In regards to the Objection to the Specification, Applicants' amendments filed April 7, 2003 have been fully considered and have overcome the Objection set forth in the Office Action dated November 19, 2002 (Specification amended).

In regards to the Objection to claim 6 under 37 CFR 1.75(c), Applicants' amendments filed April 7, 2003 have been fully considered have been fully considered but they are not persuasive. The Objection to claim 6 is maintained for the reasons of record as set forth in the Office Action dated November 19, 2002.

In regards to the Rejection of claims 1-7, 9-14, 16-35, 39, 52-55 and 59 under 35 U.S.C. 112, first paragraph, Applicants' amendments filed April 7, 2003 have been fully considered and have overcome the Rejection set forth in the Office Action dated November 19.

In regards to the Rejection of claims 1-7, 9-14, 16-35, 39-55 and 59 under 35 U.S.C. 112, second paragraph, Applicants' amendments filed April 7, 2003 have been fully considered and have overcome the Rejection set forth in the Office Action dated November 19, 2002 (claims amended or cancelled).

In regards to the Rejection of claims 1-7, 9-14, 16-35, 39-55 and 59 under 35 U.S.C. 102(b) as anticipated by ROSER et al., Applicants' amendments filed April 7, 2003 have been fully considered but they are not persuasive. The Rejection of the claims is maintained for the reasons of record as set forth in the Office Action dated November 19, 2002.

In regards to the Rejection of claims 1-7, 9-14, 16-35, 39-55 and 59 under 35 U.S.C. 103(a) as being unpatentable over ROSER in view of BAR-SHALOM, Applicants' amendments filed April 7, 2003 have been fully considered but they are not persuasive. The Rejection of the claims is maintained for the reasons of record as set forth in the Office Action dated November 19, 2002.

Response to Arguments filed April 7, 2003

Applicant's arguments filed April 7, 2003 have been fully considered but they are not persuasive.

In response to Applicants' argument that neither ROSER nor ROSER in view of BAR-SHALOM teach or suggest compositions with the requisite intrinsic strength to be useful as needles, it is noted that while ROSER does not teach specific formulations with therapeutic agents incorporated into the HDC delivery systems, ROSER does teach in the section entitled HDC Delivery Systems on page 20, line 21 to page 27, line 20, that the HDC delivery systems are particular suited for use in controlled, pulsatile or delayed release of guest substances, which may be incorporated in the HDC delivery system. See in particular page 20, lines 31-35. Further, on page 22, line 29 to page 23, line 3, ROSER teaches that the properties of HDC are easily manipulated by slight alterations in composition, i.e. by varying the modifications of a particular carbohydrate or by combining a variety of different HDCs, thus the "HDC delivery systems can be tailored to have precise properties...". It would be obvious to one of skill in the art at the time the invention was filed to modify the particular carbohydrate or combine a variety of different HDCs to achieve a delivery system that can be molded into any shape or form,

including a needle, for use in controlled, pulsatile or delayed release of guest substances. Therefore, ROSER, and thus also ROSER in view of BAR-SHALOM, provide proper motivation to make and use the recited invention.

In response to Applicants' argument that ROSER does not teach or suggest HDC compositions with the therapeutic agent distributed homogenously throughout the compositions, it is noted that while ROSER does not teach specific formulations with therapeutic agents distributed homogenously throughout the compositions, ROSER does teach on page 25, lines 15-18 that the guest substance, i.e. therapeutic agent, can be incorporated into either the pre-melted HDC formulation, or stirred into the cooling HDC melt before quenching. In addition, ROSER teaches on page 26, lines 6-8, that the guest substance can be easily incorporated either from solution or as a particle suspension. "The HDC melts are excellent solvents for many organic molecules. This makes them particularly suitable for use in delivery of bioactive materials otherwise difficult to formulate" (page 24, lines 26-29). Therefore, it would be obvious to one of skill in the art at the time the invention was filed to distribute therapeutic agents homogenously throughout the compositions as such compositions are suitable materials that are hard to formulate for controlled, pulsatile or delayed release. Therefore, ROSER provides proper motivation to make and use the recited invention.

Inventor's Declaration under 37 CFR 1.132

The Inventor's Declaration under 37 CFR 1.132 filed on August 12, 2002 is insufficient to overcome the rejection of claims 1-16 based upon U.S. Patent No. 4,141,973 to BALAZS in

view of U.S. Patent No. 5,559,104 to ROMEO et al. as set forth in the Office Action dated February 12, 2002.

In response to the argument that ROSER does not teach the threshold of drug allowable in a composition in order to obtain a needle with sufficient intrinsic strength, but rather teaches specific compositions that only contain HDC, and that a person skilled in the art would understand that HDC mixed with most common drugs would be less strong than HDC alone, it is noted that it is well known in the art, as per ROSER, that the properties of the HDC composition is easily manipulated by slight alterations in composition, i.e. by varying the modifications of a particular carbohydrate or by combining a variety of different HDCs. Therefore, the necessary intrinsic strength of the composition is readily attained by one of skill in the art, and is seen as a choice of experimental design and well within the purview of the prior art.

In the absence of objective side-by-side comparison of the unexpected success of compositions with at least 0.5% by weight of binder and greater than 25% by weight of therapeutic agent, such manipulation is considered routine to one of ordinary skill in the art and the *prima facie* case for obviousness is maintained.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Claim Objections

Claim 6 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, namely claim 3. Applicants are

required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 41 is objected to because of the following informalities: Claim 41refers to a "mould cavity" where Applicant intends "mold cavity".

Claim 55 is objected to because of the following informalities: Claim 55 refers to "immunisation" where the more accepted spelling is "immunization".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 11 is dependent upon cancelled claim 8, and is therefore incomplete.

Further, claim 11 recites the limitation "pellet". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 9-14, 16-35, 39-55 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over ROSER, previously cited.

Applicants claim solid pharmaceutical compositions having the shape of a needle for parenteral injection with (a) a binder that is at least 0.5% by weight of the composition comprising at least one non-crystallization agent and at least one carbohydrate-binding agent, and (b) at least one therapeutic agent that is at least 25% by weight of the composition, such that the therapeutic agent is distributed homogenously throughout the composition. In addition, Applicants claim compositions with specific physical properties, such as binders that can withstand a pressure force of at least 5 or 10 Newtons, binders that remain in as an amorphous matrix for at least 6 months at ambient temperature, binders with a glass transition temperature of at least 30°C and compositions with specific viscosities at a certain temperature range. Applicants also claim methods to make such compositions by mixing, shaping and cooling. Finally, Applicants claim methods for injecting such compositions using an ejection device.

ROSER as set forth in the Office Action mailed November 19, 2002, is incorporated herein as set forth supra. ROSER teaches solid dose delivery system comprising an active agent and a glassy vehicle that may be a carbohydrate. Further, ROSER teaches inclusion of sugar alcohols, which are non-crystallization agents of the claims. The composition may be formulated in various shapes, including as a needle. Any of a number of therapeutic agents may be employed. See the claims. The ROSER method or preparation (see e.g. claim 43) includes mixing, shaping and drying. Pages 6-7 of ROSER suggest administration to animals, as well as human patients. On page 7, lines 9-29, ROSER teaches that it would be advantageous to provide solid drug delivery systems of defined size, shape, density and dissolution rate, to ensure a more

uniform distribution. In addition, ROSER teaches that small delivery system size would also increase the comfort of the administration and minimize tissue damage. Further, ROSER teaches on page 24, lines 29-31 that more than 20% weight percentage of organic molecules can be incorporated into the HDC delivery systems. ROSER teaches in the section entitled HDC Delivery Systems on page 20, line 21 to page 27, line 20, that the HDC delivery systems are particular suited for use in controlled, pulsatile or delayed release of guest substances, which may be incorporated in the HDC delivery system. See in particular page 20, lines 31-35. Further, on page 22, line 29 to page 23, line 3, ROSER teaches that the properties of HDC are easily manipulated by slight alterations in composition, i.e. by varying the modifications of a particular carbohydrate or by combining a variety of different HDCs, thus the "HDC delivery systems can be tailored to have precise properties...". ROSER teaches on page 25, lines 15-18 that the guest substance, i.e. therapeutic agent, can be incorporated into either the pre-melted HDC formulation, or stirred into the cooling HDC melt before quenching. In addition, ROSER teaches on page 26, lines 6-8, that the guest substance can be easily incorporated either from solution or as a particle suspension. "The HDC melts are excellent solvents for many organic molecules. This makes them particularly suitable for use in delivery of bioactive materials otherwise difficult to formulate" (page 24, lines 26-29).

ROSER does not specifically state that the therapeutic agent should be at least 25% of the composition. In addition, ROSER may not explicitly disclose each of the ingredients or formulation details as claimed.

It would have been obvious for a person of ordinary skill in the art at the time of the invention to increase the concentrations of the therapeutic agent. ROSER teaches that more than

20% of the organic molecules can be incorporated into the delivery system. Therefore, one of ordinary skill in the art would have been motivated and had a reasonable expectation of success in making and using a composition with more than 25% weight percentage of organic molecules in the compositions to maximize the amount of therapeutic to be delivered and to minimize the size of the compositions to increase the comfort of administration and reduce tissue damage. The formulation details are considered to have been obvious in view of the overall teaching of ROSER, for the purpose of optimizing the effectiveness of the composition and of minimizing the amount of pain and tissue damage. It would be obvious to one of skill in the art at the time the invention was filed to modify the particular carbohydrate or combine a variety of different HDCs to achieve a delivery system that can be molded into any shape or form, including a needle, for use in controlled, pulsatile or delayed release of guest substances. Further, it would have been obvious to one of ordinary skill in the art to distribute therapeutic agents homogenously throughout the compositions as such compositions are suitable materials that are hard to formulate for controlled, pulsatile or delayed release. Therefore, one of ordinary skill in the art would have been motivated and had a reasonable expectation of success to make and use the specific compositions of the present invention.

Further, claims 1-7, 9-14, 16-35, 39-55 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over ROSER, in view of International Publication WO 94/22423 to BAR-SHALOM (N), both previously cited.

As set forth supra, Applicants claim solid pharmaceutical compositions having the shape of a needle for parenteral injection with (a) a binder that is at least 0.5% by weight of the

composition comprising at least one non-crystallization agent and at least one carbohydrate binding agent, and (b) at least one therapeutic agent that is at least 25% by weight of the composition, such that the therapeutic agent is distributed homogenously throughout the composition. Applicants also claim methods to make and use such compositions.

ROSER, as set forth supra, teaches solid dose delivery system comprising an active agent and a glassy vehicle that may be a carbohydrate. Further, ROSER teaches inclusion of sugar alcohols, which are non-crystallization agents of the claims. The composition may be formulated in various shapes, including as a needle. Any of a number of therapeutic agents may be employed. See the claims. The ROSER method or preparation (see e.g. claim 43) includes mixing, shaping and drying. Pages 6-7 of ROSER suggest administration to animals, as well as human patients. On page 7, lines 9-29, ROSER teaches that it would be advantageous to provide solid drug delivery systems of defined size, shape, density and dissolution rate, to ensure a more uniform distribution. In addition, ROSER teaches that small delivery system size would also increase the comfort of the administration and minimize tissue damage. Further, ROSER teaches on page 24, lines 29-31 that more than 20% weight percentage of organic molecules can be incorporated into the HDC delivery systems. ROSER teaches in the section entitled HDC Delivery Systems on page 20, line 21 to page 27, line 20, that the HDC delivery systems are particular suited for use in controlled, pulsatile or delayed release of guest substances, which may be incorporated in the HDC delivery system. See in particular page 20, lines 31-35. Further, on page 22, line 29 to page 23, line 3, ROSER teaches that the properties of HDC are easily manipulated by slight alterations in composition, i.e. by varying the modifications of a particular carbohydrate or by combining a variety of different HDCs, thus the "HDC delivery

systems can be tailored to have precise properties...". ROSER teaches on page 25, lines 15-18 that the guest substance, i.e. therapeutic agent, can be incorporated into either the pre-melted HDC formulation, or stirred into the cooling HDC melt before quenching. In addition, ROSER teaches on page 26, lines 6-8, that the guest substance can be easily incorporated either from solution or as a particle suspension. "The HDC melts are excellent solvents for many organic molecules. This makes them particularly suitable for use in delivery of bioactive materials otherwise difficult to formulate" (page 24, lines 26-29).

ROSER does not specifically state that the therapeutic agent should be at least 25% of the composition. In addition, ROSER may not explicitly disclose each of the ingredients or formulation details as claimed.

BAR-SHALOM discloses solid pharmaceutical compositions with a shape and consistency enabling it to penetrate the skin, *consisting essentially of* the active drug substance (page 6, lines 26-34). BAR-SHALOM teaches that such compositions must have the sufficient strength to enable penetration of the skin or mucosa. Therefore, various materials can be added to the compositions, including carbohydrates, such as polysaccharides, sucrose, glucose, agarose, dextrin and cyclodextrin, in crystalline or caramelized form. See page 16, line 23 to page 17, line 10.

It would have been obvious to one of skill in the art to make and use the compositions of the present invention to make and use the pharmaceutical compositions of the present invention wherein the therapeutic agent is at least 25% of the composition by weight (i.e. wherein the binder is at most 75% of the composition by weight). ROSER teaches pharmaceutical compositions comprising all of the disclosed ingredients. BAR-SHALOM teaches that such

pharmaceutical compositions require only enough binder to give sufficient strength to penetrate the skin or mucosa. The ratios of binder to therapeutic agent as well as the formulation details are considered to have been obvious over the overall teaching of ROSER in view of BAR-SHALOM, for the purpose of optimizing the effectiveness of the composition and of minimizing the amount of pain and tissue damage. It would be obvious to one of skill in the art at the time the invention was filed to modify the particular carbohydrate or combine a variety of different HDCs to achieve a delivery system that can be molded into any shape or form, including a needle, for use in controlled, pulsatile or delayed release of guest substances. Further, it would have been obvious to one of ordinary skill in the art to distribute therapeutic agents homogenously throughout the compositions as such compositions are suitable materials that are hard to formulate for controlled, pulsatile or delayed release. Therefore, one of ordinary skill in the art would have been motivated and had a reasonable expectation of success to make and use the specific compositions of the present invention.

Conclusion

Claims 1-7, 9-14, 16-35 and 39-59 are pending. Claims 56-58 are withdrawn. Claims 1-7, 9-14, 16-35, 39-55 and 59 are rejected. Claims 6, 41 and 55 are objected to. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Josephine Young whose telephone number is (703) 605-1201. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached at (703) 308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

JY
June 28, 2003

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
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